

Translation

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PATENT COOPERATION TREATY

PCT/DE2003/004136



PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 2002P20377WO	FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. PCT/DE2003/004136	International filing date (day/month/year) 15 December 2003 (15.12.2003)	Priority date (day/month/year) 19 December 2002 (19.12.2002)
International Patent Classification (IPC) or national classification and IPC C12Q 1/68		
Applicant SIEMENS AKTIENGESELLSCHAFT		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
 - a. ☐ (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows:
 - ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
 - ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
 - b. ☐ (sent to the International Bureau only) a total of _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

- | | |
|---|---|
| <input checked="" type="checkbox"/> Box No. I | Basis of the report |
| <input type="checkbox"/> Box No. II | Priority |
| <input type="checkbox"/> Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> Box No. VI | Certain documents cited |
| <input type="checkbox"/> Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> Box No. VIII | Certain observations on the international application |

Date of submission of the demand 06 July 2004 (06.07.2004)	Date of completion of this report 26 August 2005 (26.08.2005)
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International Application No.

PC1/DE2003/004136

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

- ☐ This report is based on translations from the original language into the following language _____, which is language of a translation furnished for the purpose of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on (replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):

- ☐ The international application as originally filed/furnished
- ☒ the description:
- pages _____ 1-16 _____, as originally filed/furnished
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☒ the claims:
- pages _____ 1-15 _____, as originally filed/furnished
- pages* _____, as amended (together with any statement) under Article 19
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☒ the drawings:
- pages _____ 1/6-6/6 _____, as originally filed/furnished
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (specify): _____
- ☐ any table(s) related to sequence listing (specify): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (specify): _____
- ☐ any table(s) related to sequence listing (specify): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/DE/04136

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	4, 7-10, 12, 15	YES
	Claims	1-3, 5-6, 11, 13-14	NO
Inventive step (IS)	Claims		YES
	Claims	4, 7-10, 12, 15	NO
Industrial applicability (IA)	Claims	1-15	YES
	Claims		NO

2. Citations and explanations

5.1 This report makes reference to the following documents:

- D1: WO 00/62036 A (NERENBERG MICHAEL I; EDMAN CARL F (US); WALKER GEORGE T (US); NANO) 19 October 2000 (2000-10-19)
- D2: WO 00/60919 A (FENG LANA L; LANDIS GEOFFREY C (US); NERENBERG MICHAEL I (US); EDM) 19 October 2000 (2000-10-19)
- D3: US 6258606 (KOVACS GREGORY T A)
- D4: US 5736257 (CONRAD DAVID W; CHARLES PAUL T)
- D5: WO 02/20833 (ZELTZ P, SCHEIDER S (DE))
- D6: WO 00/58522 (GILES PATRICK et al. (US))
- D7: FUCHS A ET AL: 'A SILICON LAB-ON-CHIP FOR INTEGRATED SAMPLE PREPARATION BY PCR AND DNA ANALYSIS BY HYBRIDIZATION' ANNUAL INTERNATIONAL IEEE-EMBS SPECIAL TOPIC CONFERENCE ON MICROTECHNOLOGIES IN MEDICINE AND BIOLOGY. PROCEEDINGS, 2 May 2002 (2002-05-02), pages 227-231, XP001180969.

NOVELTY:

5.2 Claim 1:

D1 discloses a method for PCR amplification and detection of nucleotide sequences that comprises the

steps (a) to (d) recited in claim 1 (D1, abstract; page 13, line 20 to page 26, line 15; claims 1-47, in particular claims 6, 15, 22, 34; figures 1, 2, 12-15, 22 and 23). Therefore, claim 1 lacks novelty in light of D1. The same applies to D2, a document that has same international filing date as D1 but does not belong to the same patent family (see D2, claims 1-32). Furthermore, D3 also discloses a method that relates to PCR amplification and detection of nucleic acids and discloses steps (a) to (d) (see D3, figures 4(c) and 7; column 3, line 5 to column 4, line 54; claims 1-24; column 8, lines 8-38), and therefore claim 1 lacks novelty also in light of this document. Finally, D6 and D7 likewise disclose this type of method (D6, claims 1-9, figure 2; D7, abstract, figures 1-4) and are prejudicial to the novelty of claim 1.

5.3 Claims 2-3:

Claim 2 lacks novelty, because D1 discloses a method that involves a hydrophilic layer with coupling groups for the covalent bonding of probe molecules (D1, page 56, lines 22-26, figure 16). Furthermore, D6 and D7 disclose this type of reaction layer (D6, page 8, lines 5-14; D7, figure 4). The same applies to claim 3, since the streptavidin layer (see above) disclosed in D1 is a "hydrogel". Therefore, claims 2 and 3 lack novelty in light of D1 or D6 and D7, respectively.

5.4 Claims 5-6:

Claim 5 lacks novelty in light of D3, since this document discloses methods that have an electronically addressable microchip, an insulating layer and a reaction layer with the corresponding

orientation (D3, figure 7). Claim 6 likewise lacks novelty, since D3 discloses silicon substrates (D3, figure 7).

5.5 Claims 11 and 13-14

D1 discloses a device comprising a biochip with a hydrophilic reaction layer, and an array of analysis positions (D1, see above). Therefore, claim 11 lacks novelty in light of D1. The same applies to D2 (D2, claims 1-32), D4 (see figures 1-4, claims 1-7, columns 4-6), D6 (claims 1-9, page 8, lines 5-14) and D7 (figures 1-4, abstract). The above-mentioned documents are also prejudicial to the novelty of claim 13, because the devices disclosed in D1-D2, D4, D6 and D7 all comprise carriers for microspots. Claim 14 lacks novelty over D4 (figures 1-5, column 6, lines 12-18), because D4 discloses semiconductor material with an insulating layer (D4, figures 4(a) to 4(c)).

INVENTIVE STEP:

5.6 Claim 4:

D1 is regarded as the closest prior art, since it serves the same general purpose as claim 4. The difference between D1 and claim 4 is that in claim 4, the nucleic acid probe is immobilized on the surface using an acrylamide gel, whereas the method disclosed in D1 uses immobilized streptavidin and biotinylated nucleic acids. The technical effect achieved thereby consists in providing an alternative immobilization possibility for the corresponding probes. Accordingly, the problem to be solved by claim 4 is that of providing a method for PCR amplification and detection of nucleic acids that is based on arrays and provides an alternative

immobilization of nucleic acids on the surface of the array or chip. The problem is solved by the method that is recited in claim 4 and based on an acrylamide gel.

5.7 D4 discloses the immobilization of biological macromolecules or nucleic acids on chip surfaces using acrylamide-based photoactivatable polymer networks (D4, claims 1-7). Since D4 mentions substrates with "patterns" of biomolecules, D4 directly suggests an application for this method based on said technique for immobilization on arrays (the term "array" corresponds to the term "pattern" used in D4; see D4, column 4, line 7 to column 6, line 3, claims 1-7). Therefore, the subject matter of claim 4 is rendered obvious by a combination of D1 and D4.

5.8 Claims 7-10:
Claims 7-10 are regarded as obvious in light of a combination of D1 (see above) and D5, since D5 discloses a nested PCR and teaches that this type of reaction can be carried out with immobilized oligonucleotides (D5, figures 1-3, claims 1-15).

5.9 Claims 12 and 15:
Claim 12 is obvious in light of a combination of D1 (see above) and D3, since D3 discloses a device that comprises a housing with through-flow (see D3, figure 6(b)). Claim 15 does not involve an inventive step, since the use of thin-layer technology in the field of semiconductor electrodes is a matter of standard practice for a person skilled in the art.